What is claimed is:

1. A method for screening for nucleic acid duplex stability by competitive equilibria comprising:

(a) producing a solution containing a known amount of an initial nucleic acid duplex with a known stability, said initial nucleic acid duplex comprising a first nucleic acid strand having a sequence wholly or in part homologous to a target strand and a second nucleic acid strand having a sequence wholly or in part complementary to the target strand;

(b) titrating the solution with a second solution comprising a known concentration of the target nucleic acid strand which competes with the first nucleic acid strand for binding to the second nucleic acid strand, said target nucleic acid strand being single- or double-stranded;

(c) subjecting the titrated solution to conditions which disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the second nucleic acid strand, but which do not disrupt the target strand when double-stranded;

(d) subjecting the titrated solution to conditions which promote duplex or triplex formation; and

(e) monitoring the titrated solution for changes in the amount of initial nucleic acid duplex formed as a function of the amount of target nucleic acid strand added.

2. The method of claim 1 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the second nucleic acid strand, but which do not disrupt the target strand when double-stranded and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

3. A method for screening for nucleic acid duplex stability comprising:

(a) producing a solution containing an initial nucleic acid duplex comprising an initial nucleic acid duplex with a known stability, said initial nucleic acid duplex comprising a first nucleic acid strand and a second nucleic acid strand, each strand being capable of forming a duplex with a double-stranded target strand;

(b) titrating the target strand into the solution to compete with initial nucleic acid duplex formation by forming duplexes of target strand and first nucleic acid strand and target strand and second nucleic acid strand;

(c) subjecting the titrated solution to conditions which disrupt the initial nucleic acid duplex, the double-stranded target strand, and any duplex between the disrupted target strands and the first and second nucleic acid strands;

(d) subjecting the titrated solution to conditions which promote duplex formation; and

(e) monitoring the titrated solution for changes in the amount of initial nucleic acid duplex formed as a function of the amount of target nucleic acid strand added.

4. The method of claim 3 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex, the double-stranded target duplex and any duplexes formed between the disrupted target strands and the first or second nucleic acid strands and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

5. A method for extracting enthalpy data from the competitive equilibria method of claim 2 or 4 comprising controlling temperature during step (d) so that changes monitored in step (e) can be collected as a function of temperature to produce a family of titration curves that can be used to extract enthalpy ($\Delta H^\circ$) data.

6. A method for detecting a single nucleotide polymorphism comprising:

(a) producing an initial nucleic acid duplex comprising a first and second nucleic acid strand, wherein the first or second strand of the duplex is designed to identify a single nucleotide polymorphism in a single- or double-stranded target nucleic acid sequence;

(b) measuring the amount of the initial nucleic acid duplex;

(c) adding a fixed excess amount of a target nucleic acid strand into the solution;

(d) subjecting the solution to conditions which disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the first or second nucleic acid strand, but which do not disrupt the target strand when double-stranded;

(e) subjecting the titrated solution to conditions which promote duplex or triplex formation; and

(f) measuring the amount of initial duplex formed after addition of the target strand wherein the measured amount after addition of the target strand is indicative of the target strand containing the single nucleotide polymorphism.

7. The method of claim 6 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the second nucleic acid strand, but which do not disrupt the target strand when double-stranded and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

8. A method for detecting a single nucleotide polymorphism comprising:

(a) producing an initial nucleic acid duplex comprising a first and second nucleic acid strand, wherein the

first or second strand of the duplex is designed to identify a single nucleotide polymorphisms in a double-stranded target nucleic acid sequence;

(b) measuring the amount of the initial nucleic acid duplex;

(c) adding a fixed excess amount of a target nucleic acid strand into the solution;

(d) subjecting the solution to conditions which disrupt the initial nucleic acid duplex, the double-stranded target nucleic acid sequence and any duplex formed between the target strand and the first or second nucleic acid strand;

(e) subjecting the titrated solution to conditions which promote duplex formation; and

(f) measuring the amount of initial duplex formed after addition of the target strand wherein the measured amount after addition of the target strand is indicative of the target strand containing the single nucleotide polymorphism.

9. The method of claim 8 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex, the double-stranded target duplex and any duplexes formed between the disrupted target strands and the first or second nucleic acid strands and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

10. The method of claims 6 through 9 wherein one nucleic acid strand of the duplex formed in step (a) contains a sequence corresponding to the targeted single nucleotide polymorphism; and the measured amount of initial duplex formed after addition of the target strand indicative of the target strand containing the single nucleotide polymorphism in step (f) decreases as compared to the amount measured in step (b).

11. The method of claims 6 through 9 wherein one nucleic acid strand of the duplex formed in step (a) is a wild type sequence; and the measured amount of initial duplex formed after addition of the target strand is indicative of the target strand containing the single nucleotide polymorphism in step (f) is approximately equal to the amount measured in step (b).

12. A method for determining the concentration of a target nucleic acid sequence comprising:

(a) adding a known volume and concentration of an initial nucleic acid duplex with a known stability to a known volume of a solution containing a target strand;

(b) subjecting the solution to conditions which disrupt the initial nucleic acid duplex and any duplex between the target strand and a strand of the initial nucleic acid duplex;

(c) subjecting the solution to conditions which promote duplex formation; and

(d) determining the relative change in the amount of initial duplex formed in the solution.

13. A method for determining the concentration of a target nucleic acid sequence comprising:

(a) adding a known volume of a solution of target strand to a known volume of a solution containing a known concentration of an initial nucleic acid duplex with a known stability;

(b) subjecting the solution to conditions which disrupt the initial nucleic acid duplex and any duplex between the target strand and a strand of the initial nucleic acid duplex;

(c) subjecting the solution to conditions which promote duplex formation; and

(d) determining the relative change in the amount of initial duplex formed in the solution.

14. The method of claim 12 or 13 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the second nucleic acid strand, but which do not disrupt the target strand when double-stranded and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

15. A method for assessing stability of various selected target strands comprising:

(a) selecting various target strands;

(b) performing the method of claim 1 with the same initial nucleic acid duplex and each of the selected target strands; and

(c) comparing monitored changes in the amount of initial nucleic acid duplex formed as a function of the amount of the selected target nucleic acid strand added to ascertain differences in stability of duplexes or triplexes formed by the various target strands.

16. The method of claims 1 through 15 wherein changes in the amount of initial nucleic acid duplex as a function of the amount of target nucleic acid strand added are monitored optically.

17. The method of claim 16 wherein fluorescent dyes are attached to the first and second nucleic acid strands of the initial nucleic acid duplex and changes are monitored optically via eximer fluorescence.

18. The method of claims 1 through 15 wherein the first nucleic acid strand comprises a donor nucleic acid strand labeled with a donor of a FET pair and the second nucleic acid strand comprises an acceptor nucleic acid strand labeled with an acceptor of the FET pair and changes in the amount of initial nucleic acid duplex in the titrated solution are monitored by measuring changes in FET donor or acceptor intensity.

19. The method of claims 1 through 4 wherein multiple distinguishably labeled initial nucleic acid duplexes are produced in step (a) and monitored for changes in step (e) or (f).

20. The method of claim 19 wherein each distinguishably labeled initial nucleic acid duplex comprises nucleic acid strands labeled with different FET pairs to differentiate so that changes can be monitored via selective fluorescence excitation with different wavelength light and detection of emission at different wavelengths.

21. The method of claim 20 wherein at least one of fluorescent dye is used as a FET donor in one duplex and a FET acceptor in another duplex.

22. The method of claim 19 wherein the multiple initial nucleic acid duplexes are produced by addition of one first nucleic acid strand which is wholly or in part homologous to the target strand and multiple second nucleic acid strands which are wholly or in part complementary to the target.

23. The method of claim 22 wherein the first nucleic acid strand is labeled with an FET donor and the multiple second nucleic acid strands are labeled with different FET acceptors.

24. The method of claim 22 wherein the first nucleic acid stand is labeled with an FET acceptor and the multiple second nucleic acid strands are labeled with different FET donors.

25. The method of any of claims 1 through 24 wherein at least one nucleic acid strand of the initial duplex comprises an internal loop, a modified base, a modified backbone, or a non-Watson-Crick nucleotide base variation.

26. The method of claim 25 wherein the modified backbone comprises peptido-nucleic acids (PNA) or oligomers incorporating modified phosphate or sugar moieties.

27. The method of claim 26 wherein the non-Watson-Crick nucleotide base variation comprises an intra strand crosslink, an abasic site, a naturally occurring or synthetic base variant, a base mimetic or a base adduct.

28. The method of claims 1 through 27 wherein at least one nucleic acid strand of the initial nucleic acid duplex is immobilized to a solid support.

29. The method of claim 28 wherein changes in initial nucleic acid duplex are monitored via surface plasmon resonance spectroscopy.

30. A method for determining the concentration of a target nucleic acid sequence comprising:

(a) measuring fluorescence of a known volume of a solution containing a single- or double-stranded target nucleic acid sequence;

(b) adding a known volume and concentration of an initial nucleic acid duplex to the solution;

(c) subjecting the solution to conditions which disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and strands of the initial nucleic acid duplex, but which do not disrupt the target strand when double-stranded;

(d) subjecting the solution to conditions which promote duplex or triplex formation; and

(e) measuring the fluorescence of the solution after step (d) so that a relative change in the fluorescence can be determined.

31. A method for determining the concentration of a target nucleic acid sequence comprising:

(a) measuring fluorescence of a solution containing a known volume and concentration of an initial nucleic acid duplex;

(b) adding a known volume of a single- or double-stranded target nucleic acid sequence to the solution;

(c) subjecting the solution to conditions which disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and strands of the initial nucleic acid duplex, but which do not disrupt the target strand when double-stranded;

(d) subjecting the solution to conditions which promote duplex or triplex formation; and

(e) measuring the fluorescence of the solution after step (d) so that a relative change in the fluorescence can be determined.

32. The method of claims 30 or 31 wherein the conditions in step (c) comprise heating the titrated solution to a temperature high enough to disrupt the initial nucleic acid duplex and any duplex or triplex formed between the target strand and the second nucleic acid strand, but which do not disrupt the target strand when double-stranded and the conditions of step (d) comprise cooling the titrated solution to a temperature wherein duplex formation occurs.

33. A kit for screening for nucleic acid duplex stability by competitive equilibria comprising a known concentration of an initial nucleic acid duplex with a known stability, said initial nucleic acid duplex comprising a first nucleic acid strand having a sequence wholly or in part homologous to a target strand and a second nucleic acid strand having a sequence wholly or in part complementary to the target strand.

34. A kit for screening for nucleic acid duplex stability comprising a FET-labeled nucleic acid duplex wherein a first nucleic acid strand of the duplex is labeled with a donor of a FET pair and a second nucleic acid strand of the duplex is labeled with an acceptor of the FET pair.

35. A kit for screening for single nucleotide polymorphisms comprising an initial nucleic acid duplex wherein the first or second strand of the duplex is designed

to identify a single nucleotide polymorphism in a single- or double-stranded target nucleic acid sequence.

36. The kit of claim 35 wherein the initial nucleic acid duplex is FET-labeled.

37. The kits of claim 33 through 36 wherein a strand of the initial nucleic acid duplex is immobilized to a solid support.